REMARKS

In response to the above-identified Final Office Action ("Action"), Applicants traverse the Examiner's rejection of the claims and seek reconsideration thereof. Claims 22-59 are pending in the present application. Claims 38 and 42-59 are rejected. In this response, claims 38 and 57 are amended, claims 22-37, 39-41, 58 and 59 are cancelled and no claims are added.

I. Claim Amendments

Applicants respectfully submit herewith amendments to claims 38 and 57. Claim 38 is amended to recite a method for depigmenting or bleaching human skin, body hair and/or hair of the head of a subject "to lighten the color for purely cosmetic purposes comprising the topical application to the skin, body hair and/or hair of the head of said subject of a cosmetic composition." Support for the amendments to claim 38 may be found, for example, at page 4, lines 23-29 of the Application. Claim 57 is amended to recite that the treatment is for particular hyperpigmentation disorders in subjects in need thereof and to the topical application to hyperpigmented skin areas of said subjects.

Applicants respectfully submit the amendments are supported by the specification and do not add new matter. Accordingly, Applicants respectfully request consideration and entry of the amendments to claims 38 and 57.

II. Claim Rejections – 35 U.S.C. §102

In the Action, claims 38 and 42-57 are rejected under 35 U.S.C. §102(b) as being anticipated by International Publication No. WO 95/02069 issued to Bennett et al. ("Bennett") as evidenced by *The Use of Antisense Strategy to Modulate Human Melanogenesis* by Lazou et al. ("Lazou").

It is axiomatic to a finding of anticipation that each and every element of the rejected claim be found within a single prior art reference.

In regard to independent claims 38 and 57, Applicants respectfully submit that Bennett as evidenced by Lazou fails to teach a method for depigmenting or bleaching human skin, body hair

and/or hair of the head "of a subject ***to lighten the color for purely cosmetic purposes*** comprising the topical application ***to the skin, body hair and/or hair of the head of said subject*** of a cosmetic composition comprising at least one oligonucleotide containing between 7 and 25 nucleotides, capable of specifically hybridising with genes or gene products coding for protein kinase C beta-1 (PKC beta-1)" (emphasis added) as recited in amended claim 38 and a method for the "treatment of regional hyper-pigmentation by melanocyte hyperactivity such as idiopathic melasma, local hyper-pigmentation by benign melanocyte hyperactivity and proliferation such as pigmentary age spots (actinic lentigo), accidental hyper-pigmentation such as photosensitization or post-lesion healing ***in a subject in need thereof, comprising the topical application to the hyperpigmented skin areas of said subject***" (emphasis added) as recited in amended claim 57.

In regard to claim 38, claim 38 now recites that the depigmenting or bleaching applies to the skin, body hair and/or hair of the head of subjects to lighten the color for purely cosmetic purposes and to the topical application to the skin or hair of such subjects.

The Examiner first alleges the method of claims 37-53 of Bennett relates to a method of modulating the expression of PKC in cells, in which the cells are contacted with an oligonucleotide specifically hybridizable with a PKC gene or PKC mRNA and claim 49 specifyies an oligonucleotide with a sequence identical to SEQ ID NO: 1 of the present application and thus specifically hybridizes with PKC beta I.

Thus, claim 49 relates to a method of modulating the expression of PKC in cells in which the cells are contacted using an oligonucleotide specifically hybridizable with PKC beta 1 gene or mRNA.

Claim 49, however, only teaches a method for modulating the expression of PKC in cells, and the cells in which the expression of PKC beta 1 is modulated are not defined more precisely.

In this regard, Applicants wish to draw the Examiner attention to the fact that Bennett includes several types of applications of oligonucleotides specifically hybridizable with a PKC gene or mRNA.

One of such applications relates to research tools (see Bennett, page 6 lines 4-11; page 9, line 28 to page 10, line 2; and page 17, lines 17-32), including methods for modulating PKC expression or determining PKC expression in cells or tissues (see page 9, lines 28-31).

In view of the foregoing, one of ordinary skill in the art would understand that the methods of claims 37-53 of Bennett relate to research tools for in vitro purpose and not to therapeutic or cosmetic methods applied to the human body.

In addition, Bennett never mentions or contemplates that the methods of claims 37-53 may be applied on the skin or hair of a human being.

In contrast, claim 38 of the instant Application is limited to the case in which the cosmetic composition comprising an oligonucleotide specifically hybridizable with PKC beta 1 gene or mRNA is applied topically to the skin or hair of a human subject.

As a result, claim 49 of Bennett does not disclose every method step of instant claim 38 of the present Application and thus clearly does not explicitly, or even inherently, anticipate claims 38 and 42-56.

The Examiner also refers to claims 70-94 of Bennett, which relate to a method of treating a condition associated with expression of PKC using an oligonucleotide specifically hybridizable with a PKC gene or PKC mRNA.

In the Action, the Examiner indicates that she estimates that these claims, and particularly claims 72 (psoriasis), 76 (skin cancer), 89 (PKC beta) and 90 (SEQ ID NO:28 identical to SEQ ID NO:1 of the present Application and thus specifically hybridizing with PKC beta 1), disclose the use of an oligonucleotide specifically hybridizing with PKC beta 1 in the treatment of psoriasis and skin cancer. Applicants once more respectfully disagree with this view.

Claims 72 and 76 depend on claim 71 (PKC associated condition = hyperproliferative disorder), which only depends on claim 70 (general method) and recites that the condition may be psoriasis or skin cancer, respectively.

Claims 72 and 76 thus concern methods of treating psoriasis or skin cancer, respectively, using an oligonucleotide specifically hybridizable with a PKC (in general, without indicating a particular PKC isozyme) gene or mRNA.

Claims 72 and 76 thus teach that psoriasis and skin cancer may be treated using an oligonucleotide specifically hybridizable with a PKC gene or mRNA in general, without indicating to which PKC particular isozyme said oligonucleotide should be specifically hybridizable.

Claim 90 only depends on claim 89 (PKC beta isozyme), which only depends on claim 85 (a specific PKC isozyme), which only depends on claim 70 (general method), and indicates that the oligonucleotide sequence may be SEQ ID NO:28, which is alleged to be identical to SEQ ID NO:1 of the present Application and thus specifically hybridizes with PKC beta 1.

Claim 90 thus teaches that an oligonucleotide specifically hybridizable with PKC beta 1 gene or mRNA may be used in treating a condition associated with expression of PKC in general, without indicating which particular condition is to be treated.

The important point is that in the claims, claim 90 using an oligonucleotide specifically hybridizable with PKC beta 1 gene or mRNA is not, even indirectly, dependent on claims 72 or 76 directed to the particular treatment of psoriasis and skin cancer.

In addition, in the specification of Bennett, psoriasis or skin cancer are never mentioned to be associated with an increase of PKC beta 1 expression.

As detailed in Bennett (see page 4, lines 8-10) and the document titled *Protein Kinase C isoenzymes: divergence in signal transduction?* by Hug et al (see page 330, left column lines 3-5) submitted with the information disclosure statement dated May 5, 2008, the PKC family includes a great number of distinct isozymes, with various biological properties and expression patterns.

In addition, Bennett also indicates that different PKC isozymes may be involved in various diseases (see page 4, lines 8-9), and that it is desirable to inhibit specific PKC isozymes as treatment for diseases associated with particular isozymes (see page 5, lines 7-9).

As a result, it is already clear from Bennett that PKC represents a complex family of isozymes and that particular PKC associated conditions are actually associated to one or more specific PKC isozymes and that an effective treatment will not be obtained using antisense oligonucleotides specifically hybridizable with any PKC isozyme but only using antisense oligonucleotides specifically hybridizable with the adequate PKC isozyme.

Since in the claims, claim 90 using an oligonucleotide specifically hybridizable with PKC beta 1 gene or mRNA is not, even indirectly, dependent on claims 72 or 76 directed to the particular treatment of psoriasis and skin cancer, Bennett could thus be considered as disclosing the use of an oligonucleotide specifically hybridizable with PKC beta 1 gene or mRNA for treating psoriasis or skin cancer only if there was a teaching in the specification that psoriasis and skin cancer are associated with an increased expression of PKC beta 1.

This is not the case. Concerning skin cancer, there is no description in Bennett specification of an association with an increased expression of any PKC isozyme. Only a reference to PKC in general is provided (see page 2 lines 31¬33).

Concerning psoriasis, Bennett only describes that PKC in general may be implicated (see page 2 line 31 to page 3 line 14), and that an alteration of the ratio between PKC α and PKC β has been observed in psoriatic lesions, with a loss of PKC ß compared to normal skin (see page 4, line 10-15).

Psoriasis is thus not associated with an increased expression of PKC beta 1, since only a loss of PKC beta in general (not PKC beta 1) is mentioned. In addition, since PKC beta is already underexpressed in psoriatic lesions, PKC beta does not appear as a suitable target for antisense technology in the treatment of psoriasis.

Thus, Bennett discloses that: (i) various unspecified PKC associated conditions may be treated using an oligonucleotide specifically hybridizable with PKC beta 1 (claim 90), and (ii) psoriasis and skin cancer may be treated using oligonucleotide specifically hybridizable with an unspecified particular PKC isozyme.

However, Bennett does not teach that psoriasis and skin cancer may be treated using an oligonucleotide specifically hybridizable with PKC beta 1.

Even if the Examiner considered the above arguments non persuasive and still estimated that Bennett actually teaches that psoriasis and skin cancer may be treated using an oligonucleotide specifically hybridizable with PKC beta 1, it would still not anticipate the method of claim 38.

Indeed, Bennett would then only disclose the application to the skin of subjects suffering from these disorders of a composition comprising an oligonucleotide specifically hybridizable with PKC beta 1.

In particular, claim 38 recites application of the composition to skin to lighten the color for purely cosmetic purposes. Such subjects are distinct from those suffering from psoriasis and skin cancer as disclosed in Bennett.

Thus, Bennett does not teach the step of applying a composition comprising an oligonucleotide specifically hybridizing with PKC beta 1 gene or gene products to the skin or hair of subjects to lighten their color for purely cosmetic purposes.

Regarding independent claim 57, claim 57 is directed to the treatment of subjects suffering from the claimed hyperpigmentation disorders and to the application of the composition to hyperpigmented skin areas.

Concerning claim 49 of Bennett, the arguments developed for instant claim 38 still apply. In particular, Bennett fails to disclose that the methods of claim 49 are applied to particular skin areas.

Concerning claims 70-94 and particularly claims 72, 76 and 90 of Bennett, Applicants maintains the above argument that they do not disclose the treatment of psoriasis or skin cancer using an oligonucleotide specifically hybridizable with PKC beta 1 gene or mRNA.

In addition, even if the Examiner disagreed with this view, Bennett would still not anticipate amended claim 57.

In particular, amended claim 57 recites the application to hyperpigmented skin areas of subjects suffering from various hyperpigmentation disorders (regional hyper-pigmentation by

melanocyte hyperactivity such as idiopathic melasma, local hyper-pigmentation by benign melanocyte hyperactivity and proliferation such as pigmentary age spots (actinic lentigo), accidental hyper-pigmentation such as photosensitization or post-lesion healing).

These pathologies are distinct from psoriasis and skin cancer as disclosed in Bennett, and psoriatic or skin cancer lesions are clearly distinct from claimed hyperpigmentations.

Indeed, psoriasis is an inflammatory skin condition characterized by an accelerated growth of skin cells, leading to patches of raised, reddish skin covered by silvery-white scale (see article titled *What is Psoriasis?* attached herewith). The reddish colour of psoriatic lesions is linked to inflammation of the skin. In contrast, hyperpigmentation is caused by increased melanin production and leads to a brown or black colour.

Concerning skin cancer, it is not necessary linked to pigmentation variations. Indeed, skin cancer is a general term referring to various kinds of skin neoplasia, including basal cell carcinoma and squamous cell carcinoma, which do not involve pigmentation variations (see, for example, the Wikipedia article on skin cancer enclosed herewith).

Among skin cancer, the only cancer involving pigmentation variations is melanoma, in which melanocytes, which are responsible for melanin synthesis, display uncontrolled cell growth. However, melanoma is not mentioned in Bennett.

In addition, hyperpigmentation due to melanoma is distinct from claimed hyperpigmentations. In particular, hyperpigmentation due to melanoma is caused by increased melanoma proliferation, and is thus clearly distinct from regional hyper-pigmentation by melanocyte hyperactivity.

It is also distinct from local hyper-pigmentation by benign melanocyte hyperactivity and proliferation, since melanoma is clearly not benign.

As a result, the method of amended claim 57 includes the step of applying a composition comprising an oligonucleotide specifically hybridizing to PKC beta 1 gene or mRNA to particular skin areas of subjects who are distinct from those allegedly treated in Bennett. This step is thus not disclosed in Bennett.

Consequently, the method of amended claim 57 is not anticipated by Bennett.

In addition, Bennett never associates PKC beta 1 isozyme with the control of skin or hair pigmentation. Indeed, as mentioned above, neither psoriasis nor skin cancer are described as associated with an overexpression of PKC beta 1. In addition, neither psoriasis nor skin cancer in general are conditions associated with pigmentation variations and these pathologies are only referred to as hyperproliferative diseases in Bennett.

Thus, for at least the foregoing reasons, Bennett fails to teach each and every element of claims 38 and 57. Since each of the elements of the claims are not found within the cited prior art, claims 38 and 57 are not anticipated by the cited prior art reference. Applicants respectfully request reconsideration and withdrawal of the rejection of claims 38 and 57 under 35 U.S.C. §102 over Bennett as evidenced by Lazou.

In regard to claims 42-56, these claims depend from claim 38 and incorporate the limitations thereof. Thus, for at least the reasons that claim 38 is not anticipated by Bennett, claims 42-56 are further not anticipated by the cited prior art reference. Applicants respectfully request reconsideration and withdrawal of the rejection of claims 42-56 under 35 U.S.C. §102 over Bennett as evidenced by Lazou.

III. Claim Rejections – 35 U.S.C. §112

In the Action, claims 58 and 59 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

Claims 58 and 59 are cancelled herein thereby rendering the rejection of these claims moot.

CONCLUSION

In view of the foregoing, it is believed that all claims now pending are in condition for allowance and such action is earnestly solicited at the earliest possible date. If there are any additional fees due in connection with the filing of this response, please charge those fees to our Deposit Account No. 02-2666. Questions regarding this matter should be directed to the undersigned at (310) 207-3800.

Respectfully submitted,

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Dated: October 3, 2008

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CERTIFICATE OF TRANSMISSION

I hereby certify that this correspondence is being submitted electronically via EFS Web to the United States Patent and Trademark Office on October 3, 2008.

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